^{18}FDG-PET: a new diagnostic approach in hip prosthesis infection

LA ^{18}FDG-PET: una nueva aproximación diagnóstica en la infección protésica de cadera

E. García-Barrecheguren[a], M. Rodríguez Fraile[b], G. Toledo Santana[c], J.R. Valentí Nín[a] and J.A. Richter Echevarría[b]

[a]Department of Orthopaedic Surgery and Traumatology.
[b]Department of Nuclear Medicine.
[c]Department of Pathologic Anatomy.

Clínica Universitaria de Navarra. Pamplona. Navarra.

Correspondence:
E. GARCÍA-BARRECHEGUREN
Avda. Aragón, 43, 4.º A 44600 Alcañiz. Teruel. España
E-mail: egbarreche@yahoo.es

ABSTRACT

Infection following hip arthroplasties can present a diagnostic challenge. No test is 100 % sensitive and 100% specific; this prospective study was undertaken to evaluate the utility of FDG-PET imaging for diagnosing infected joint replacements. 24 hip joint replacements were studied prospectively and we have complete diagnoses with clinical signs and symptoms, laboratory tests, radiography, joint aspiration, radionuclide imaging including FDG-PET, and histopathologic examination. 11 of 24 prostheses were infected. The sensitivity and specificity of PET for detecting infection associated with prostheses were 64.3% and 64.7% respectively, in our study.
FDG imaging is not useful in patients with suspected prosthetic infection as a screening test.
Key words: infection, septic and aseptic loosening, failed prostheses replacements, FDG-PET.

RESUMEN

Objetivo. Las causas más frecuentes de prótesis dolorosas son la movilización o aflojamiento aséptico, y la movilización séptica o infección. Una infección protésica siempre constituye un reto diagnóstico puesto que, salvo ante la presencia de fístula u otros signos de infección evidente, no existe ninguna prueba definitiva (sensibilidad y especificidad del 100%) para el diagnóstico prequirúrgico. El objetivo de nuestro estudio fue intentar conseguir un protocolo diagnóstico eficaz y eficiente de movilización protésica.

Material y método. Para ello se estudiaron 24 recambios protésicos de cadera prospectivamente mediante clínica, estudios de laboratorio, radiografía, tomografía por emisión de positrones con 2-^{18}F-fluoro-2-desoxi-D-glucosa (^{18}FDG-PET), cultivo de líquido articular y de biopsia y estudio histopatológico.
Resultados. 11 de las 24 prótesis estaban infectadas. La sensibilidad y especificidad de la tomografía por emisión de positrones (PET) para detectar infección protésica fue del 63,6 y del 61,5%, respectivamente.
Conclusiones. La imagen ^{18}FDG-PET no permite discernir, en nuestras manos, entre movilización séptica y aséptica protésica, por lo que en pacientes con sospecha de infección tiene un valor limitado como técnica de cribaje diagnóstico.
Palabras clave: infección, movilización protésica séptica y aséptica, recambios protésicos, ^{18}FDG-PET.

INTRODUCTION

As Laskin stated in 1999, "Infection as the main cause of a painful hip prosthesis (THP) should prevail over all hypotheses and before any other cause, we should think of a low profile infection" In the same way, various studies have suggested that a painful knee prosthesis (TKP) should be considered infectious until another cause is shown.[1-5]
The infection rate in primary TKPs varies between 1 and 4%,[6] and is the most common cause of failure of posterior stabilised TKP.[3] With respect to THPs, Hanssen and Rand related a rate of deep infection of 1.3% in almost 25,000 patients who underwent this operation in the Mayo Clinic (1969-1996); most of the infections took place during the first three months, with a tendency to decrease to a constant figure of 2% over the two years of evolution. For the TKPs, the figure rises to 2.5% of a total of 16,000 arthroplasties.[7] Moreover, it should be taken into account that the percentage of recurrence of infection, after replacing a septic prosthesis, is higher than after an aseptic mobilisation (for these latter cases around 3.2% for revision of the THPs and 5.6% for the TKPs) and especially after primary prosthesis surgery, since it goes on to reach percentages, according to the series, from 10 to 26% of infection with an increase in risk as the years go by.[8]

Acute infection of an arthroplasty is obvious, but the diagnosis of sub-acute or chronic infections is more problematic[6, 9-14] and supposes a bigger challenge for the orthopaedist; they are not generally associated with systemic symptoms of infection and often go unnoticed. To this has to be added the different management of the two types of mobilisations (prosthetic replacement in a single operation for aseptic mobilisations or in two halves with/without local antibiotic release systems and prolonged post-operative systemic antibiotherapy, with/without allografts or even arthrodesis, resection arthroplasty... for prosthetic infections), which can lead to failure of the prosthetic replacement (if it had) if the diagnosis is not correct, with the socioeconomic consequences that this entails[8, 15-17] (fig. 1). The estimated cost of each treatment of an infected arthroplasty in 1995 was between 50-60 thousand dollars, which in the U.S. means a national expenditure of between 200 and 250 million dollars annually.[18] The estimated expenditure in the United Kingdom, with approximately 50,000 THP annually and around 500 cases of infection in 1990, is £16 million per year.[8]

The differential diagnosis between septic and aseptic loosening is therefore fundamental, both for choosing the correct treatment and for assessing its evolution and,

sometimes, the diagnosis of safety is not reached until removal and study of the prosthetic material. Clinical suspicion (pain, local signs, general signs), radiology, scintigraphy, laboratory tests, articular punction-biopsy, other complementary tests or the combination of them do not reach 100% diagnostic sensitivity (Se) and specificity (Sp) values, and there is no universally accepted diagnostic protocol. Although the rate of infection has gradually decreased in the last thirty years,[8, 15, 16, 19-23] the problem continues to be significant because of the increasing number of arthroplasties, mainly due to the increase in the average age of the population.

Imaging tests with radiopharmaceutical agents can provide us with diagnosis of the prosthetic mobilisation; however, its use is limited due to the cost of the tests, the time necessary to perform them and especially, because they do not always give sufficient Se and Sp levels as diagnostic tests.[16, 24] Basically, for a painful prosthesis, the radiopharmaceutical agents used are: Technetium (^{99m}Tc-MDP, ^{99m}Tc-HMPAO, ^{99m}Tc-IGH), Gallium (^{67}Ga) and Indium (^{111}In-oxine, ^{111}In-IGH).

When the study was carried out with ^{111}In-oxine in cases which were positive for ^{99m}Tc-MDP, a diagnostic Se for infection of 100% and Sp of 98% was achieved in some series.[25, 26] The use of human immunoglobulin labelled with ^{99m}Tc or with ^{111}In seems to improve the results of ^{111}In-IGH with respect to the combination of ^{99m}Tc-MDP + leucocytes-^{111}In-oxine, even as an isolated test, but there are no comparative studies of both techniques in prosthetic infections exclusively, so their systematic use in daily practice is not recommended.

At the present time, the recommended sequence is the study with ^{99m}Tc-MDP + leucocytes-^{111}In-oxine, but without considering the results as definitive,[15, 16, 24, 27-31] and it is especially useful in those cases where the laboratory tests or cultures for taking of previous antibiotics are equivocal.[32]

The use of the combination of dynamic bone scintigraphy (3 phases) + labelled leucocytes is accepted as a method which has good diagnostic efficacy (between 79 and 100%) for infectious processes in the peripheral skeleton at the clinical level.[33, 34] However, the efficacy of this strategy decreases in the presence of:

1. Low-grade/subclinical infections (lower Se).[35-37]
2. Infection of adjacent soft tissues because of limited image resolution (lower Se and Sp).[27, 36]
3. Involvement of the central skeleton due to the presence of normal bone marrow and the possible presence of “cold lesions” or photopenic areas (lower Se and Sp).[27, 30, 35, 36, 38, 39]
4. Trauma or surgical operations due to the presence of ectopic haemopoietic bone marrow foci (lower Sp).[27, 36]
5.

Furthermore, if in some infection situations, two and up to three different scintigraphy techniques are required to increase the diagnostic Se and/or Sp, it is logical to think that this strategy is not very practical, since it raises the costs and the time consumed and increases the patients’ exposure to radiation; it is therefore important to find a method with the same Se and Sp in a single process.

Because of all this, positron emission tomography with 2-^{18}F-fluoro-2-deoxy-D-glucose (^{18}FDG-PET) is being proposed as a promising imaging technique in the study of musculoskeletal infections[27] and within these, in the field of prosthetic infection.[40-45]

The objective of this study is to be able to establish an effective and efficient diagnostic protocol for prosthetic mobilisation through the prospective evaluation of clinical, microbiological, imaging (including ^{18}FDG-PET) and histopathological findings and the relationship between them.

MATERIAL AND METHOD

A prospective review was carried out on 24 hip prosthesis replacements with more than six months evolution from their implantation (in different hospital centres), which were performed in our centre in a period of approximately four years (1999-2003). These constituted the case group. Of the 24 patients, 12 were men and 12 women, with ages between 37 and 81 years (mean of 67.8 years). The replacement made was one of the components (cotyloid cup or stem) or both. In all patients, there were clinical and/or radiological criteria for prosthetic mobilisation, although not always for septic loosening, so a battery of tests was requested on all patients according to the protocol: full blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), radiography of anteroposterior (AP) hips, positron emission tomography (PET) of the hips, joint fluid and biopsy sample culture and polymorphonuclear leukocyte (PMN) count in intraoperative biopsy (frozen sections). Those patients with any pathology which could alter the laboratory tests, cell composition of the prosthetic interface to be studied or imaging tests were previously removed from the sample. Likewise, those patients in whom the battery of scheduled tests could not be completed or in whom a post-operative diagnosis of the type of mobilisation (septic or aseptic) could not be reached with certainty were excluded. This definitive diagnosis, which constitutes our diagnostic gold standard, is based on confirmation of the infection on the basis of modified Tsukayama et al's criteria, 1996:

1. The same microorganism grows in at least two cultures obtained by aspiration and/or debridement.
2. The microorganism grows in a single culture associated with one of these three situations:
    a) Fistula with active drainage.
    b) Purulent drainage at the time of debridement ("poor appearance" of the tissues is not sufficient).
    c) Evidence of acute or subacute purulent inflammation on biopsy of intraarticular tissue.

It was necessary to establish this definitive diagnosis with complete confidence, so other paragraphs were added to Tsukayama's criteria, since the cultures have not always proven to be the best gold standard:

1. Poor presurgical evolution of the prosthesis in the medium term (1 year) without a justified cause (decementation, dislocation, fracture, etc.) and definitive histopathological diagnosis of acute purulent inflammation post-surgery.
2. Poor postsurgical evolution of the prosthesis in the medium term (1 year) without a justified cause (decementation, dislocation, fracture, etc.) and definitive histopathological diagnosis of acute purulent inflammation post-surgery.

Positron emission tomography equipment

Patients required previous preparation, as per the Department of Nuclear Medicine protocol, to guarantee good imaging quality. It included a 6-8 hour fast, analysis of serum glucose levels and avoiding physical exercise previously.
The radiotracer used was ^{18}FDG, the isotope of which is a positron emitter ($^{18}F^-$), and which was obtained in a cyclotron model Cyclone 18-9-IBA. 6.2 MBq/kg was administered endovenously in the forearm. The recommended dose for adults is between 10 and 15 mCi (4-6 mCi for image acquisition in 3D), although it depends on the equipment.

A minimum of 40 minutes elapsed after injection of the ^{18}FDG, since it is advisable to wait up to 50-60 minutes to reach a maximum stable glucose incorporation rate. Oral and/or intravenous hydration of the patient was carried out after injection of the ^{18}FDG, carrying out bladder catheterization (Foley catheter) and the administration of furosemide (0.25 mg/kg). In addition, in some cases, the bladder was filled retrogressively with physiological serum to remove possible artefacts caused by the activity of the ^{18}FDG filtered in the concentrated urine over the course, serving also as an anatomical reference.

Acquisition of the studies

Instrumentation
The PET tomograph used in our study was Siemens® model ECAT EXAT HR +. The axial view field was 15.5 cm, with a tomographic section thickness of 1 cm. It was acquired for 10 minutes per bed (space travelled by the bed in each movement, 13.5 cm), with 3 beds required to completely scan the patient with THP.

The emission-transmission images thus obtained were processed by OSEM iterative reconstruction (ordered subsets-expectation maximization: 1 iteration, 30 subsets) and an attenuation corrected image was obtained which allowed the standardized uptake value (SUV) to be calculated. The images were viewed in the different planes: axial, sagittal and coronal.

Semi-quantitative measurements of the concentration of the radiopharmaceutical agent in the body were taken from the tomographic images obtained from the positron emission using SUV units, after control of possible sources of error, such as the system resolution itself, the presence of accidental coincidence or dispersion phenomena, the error due to dead time and that caused by the attenuation. Attenuation acquisition was first carried out, then the transmission image was acquired, from which we obtained the SUVs and finally, the emission image was acquired.

The SUV was calculated from the formula:

$$\text{SUV} = \frac{\text{Tissue concentration (Bq/ml)}}{\text{Injected dose (Bq)/Body weight (g)}}$$

Interpretation

The increased uptake foci were qualitatively analysed according to the Gruen and De Lee zones (figs. 2A and 2B). Semi-quantitative analysis was subsequently performed by obtaining the SUV (Maximum SUVs [SUVmax]) in the hypermetabolic foci of the regions of interest (ROI).

Presurgical diagnoses of the type of mobilisation were established based on the PET images (visual interpretation) of each patient and divided into 3 categories:

1. No infection (aseptic mobilisation): pattern of uptake normal (defined in the control group) or in any other location with an intensity similar to the contralateral end or similar to/less than the synovial structures or adjacent soft tissues.
2. Possible infection (possible septic mobilisation): uptake in areas of normality with intensity much higher than the synovial structures or adjacent soft tissues or uptake in the prosthesis-bone interface with intensity greater than the synovial structures or adjacent soft tissues.
3. Certainty of infection (septic mobilisation): uptake in the prosthesis-bone interface with intensity much higher than the synovial structures or adjacent soft tissues or fistulous tract uptake.

These diagnoses were made by two independent observers (Department of Nuclear Medicine) without knowledge of the patients or of their clinical-radiological characteristics.

A control group was set up which was composed of 14 patients with THP who had been operated on in our centre (2002-2003) consecutively, who did not present postoperative incidences and who also agreed to routine control radiographies, an ^{18}FDG-PET at two months and a year after the arthroplasty, coinciding with their review consultations and laboratory tests at a year, similar to that carried out in the case patients (replacement). These studies served to establish the normal PET image uptake pattern and to be thus able to evaluate the pathological pattern. All the imaging studies, including the PET, were evaluated based on a series of areas or zones according to Gruen and DeLee[46, 47] for the THP, modified for this study: I-VII for the stem, A2-C2 for the femoral neck and A1, B and C1 for the cotyloid cup (figs. 2A and 2B).

Statistical methods

The association between qualitative variables was studied using contingency tables. Since the sample size per box was insufficient for asymptotic approximation using Chi-squared tests, the significance was assessed using exact tests, calculated using the program Exact2xK.exe from the statistical package PEPI 4.0 [Abramson JH, 2001]. Computer Programs for Epidemiologists: PEPI Version 4.0. Sagebrush Press, Salt Lake City). For the quantitative variables, the comparison between two independent groups (septic and aseptic mobilisation) was performed using Mann-Whitney U tests. The comparison between paired data (controls at two months and one year) was carried out using Wilcoxon sign rank tests. Various statistical techniques were used for the diagnostic efficacy:

1. For qualitative or quantitative variables already dichotomised: calculation of the Se, Sp and positive and negative predictive values, together with their respective

confidence intervals. The statistical package PEPI 4.0, program Scrn.exe, was used for this.

2. Determination of the diagnostic efficacy of the quantitative variables and their optimal cut-off point using ROC curves. The maximum Youden index was used as a criterion to find the optimum cut-off point.
3. Agreement of the two observers between each other and with the gold standard: kappa index. The statistical package PEPI 4.0, program kappa.exe, was used for this.

For the descriptive study and most of the statistical analyses (except those carried out with PEPI 4.0) the statistical package SPSS, v11.5 for Windows (SPSS inc. 1989-2002, Chicago-Illinois) was used.

RESULTS

We assessed which uptake areas appeared on the PET and what signal intensity (SUVmax) they had in the two groups. The results obtained are summarised in a table where the frequencies of uptake of each area are represented in percentage, as is the frequency with which these areas coincide with the SUVmax area and the relationship with the uptake of the control group for the THP (table 1).

From these results, it emerges that the uptake in the cotyloid cup (A1, B and C1) looks like a specific pattern or is related with the mobilisation, but regardless of whether it is septic or aseptic. Although C1 seems to be exclusive to the aseptic loosenings, the sample size does not allow us to confirm this with statistical significance. The uptake in the neck of the prosthesis (A2 and C2) occurs in practically 100% of the controls and in very high percentages in both areas, both for septic and aseptic mobilisations, so they are not discriminative uptake areas.

In the femoral stem, there was no uptake in any patient in our series of cases or of controls in areas 3, 5 and 6; the uptake in zones 2 and 4 is anecdotal, since there was only one case in each, but it drew attention because they did not appear in any control or in any aseptic loosening. In area 1, corresponding to the greater trochanter, it seems slightly more common in the mobilisations, but the percentages are inconclusive. Zone 7, the minor-calcar trochanter, appears as a mobilisation pattern exclusively and not in controls, but it is a datum with little weight since it does not correspond to more than one case for each type of mobilisation.

With respect to SUVmax from the same table (table 1), it emerges that in 73.9% of the cases this is located in the areas of the femoral neck, either in the external or medial zone; this finding also occurs in the control group, so it is not considered discriminative. Table 2 summarises the data on the number of uptake areas for the THPs in relation to each subgroup, septic and aseptic mobilisation, in case diagnostic discrimination is possible in relation to the number of areas. The SUVmax frequency results are also shown. Taking the type of mobilisation into account, it appears from this table (table 2) that the differences both for the number of areas and for the SUVmax do not reach statistical significance and are not clinically relevant. Therefore, neither the number of areas nor the SUVmax are useful for distinguishing between septic and aseptic mobilisation.

We have not found any statistically significant or clinically useful relationship which explains the false positive (FP) or false negative (FN) results of PET imaging in the diagnosis of septic mobilisation: neither the number of areas of osteolysis nor the amount of bone stock lost (for FP); nor the presence of periosteal detachment (for FP); nor the presence of a specific interface, such as for example, a chronic inflammation reaction to a foreign body, with an abundance of giant cells (for FP); nor taking previous antibiotics (for FN; none of the patients wrongly diagnosed as aseptic mobilisation by PET had previously taken antibiotics). Therefore we must assume that they are the FP and FN of the test itself, inherent in it.

If we perform statistical analysis of the PET as a diagnostic test of septic mobilisation in our series (table 3), we seen that the values produced by PET as regards the diagnostic efficacy are low, and do not reach good standards for its clinical application, since other tests have better diagnostic efficacy (table 4).

DISCUSSION

Since 1996, it has been suggested in the literature that the use of PET could be useful in the diagnosis of infections; the authors have based this on the observation that granulocytes and mononuclear cells use glucose significantly during the intense metabolic process in the fight against infection. This process only occurs if the white cells are activated by the humoral agents which take part during the infection. Haemopoietic bone marrow is barely seen on the FDG-PET scan because the white cells-neutrophils in it are, under normal conditions, in a state of inactivation.[36]

Therefore in the first place, in order to diagnose a bone infection (osteomyelitis), we need the imaging method, such as FDG-PET, to be able to clearly distinguish between normal bone marrow and activated white cells.

Secondly, the lesion should be able to be seen, whether it is an acute or chronic process. Thirdly, FDG, since it is a small molecule, can quickly appear in poorly perfused tissues in contrast with labelled granulocytes, which also means, in the latter case, delaying obtaining the images at least 24 hours.

In fourth place, the method has a much higher spatial resolution and is itself "tomographic", so it can distinguish whether the soft tissues have been affected or not, and it is not influenced by the presence of metallic artefacts such as happens in the case of magnetic resonance.[27, 37, 48, 49]

Finally, although PET has a high cost compared with the existing alternatives, its efficacy is superior and the leukocyte and antibody markers are pharmaceutical medicinal products which are expensive in comparison to the price of the FDG. Moreover, in a defined area of the body (for example, thigh or knee) the study could be done in 15-20 minutes, unlike tumour staging studies which require much more time, which would lower the costs.[36]

The shortage of publications inspired us to carry out a research project on prosthetic mobilisation, the diagnosis by PET and the usefulness of other tests classically used for such a purpose; it is presently the only study which we have found which is prospective,

presents homogeneous case and control groups and has histopathological and microbiological studies in all cases.

According to some authors,[44, 45] since uptake does not appear in the bone-prosthesis interface or in aseptic mobilisations in the control groups, this should be considered as a very suggestive sign of infection in a painful THP. According to this criterion, the uptake around the femoral neck is not suggestive of infection, and for other authors the aseptic mobilisation has a similar pattern,[42, 44] which would indicate that post-surgical changes (which remain for a long time) and aseptic mobilisation may be indistinguishable using this imaging method.[44, 45]

Manthey et al, 2002, established the uptake of FDG in certain areas as exclusive of infection and differentiated them from areas of synovitis and/or aseptic loosening.[40] They established the diagnosis of non-specific synovitis when there was an increase in FDG uptake in the synovial structures or soft tissues around the prosthesis compared with the contralateral side. They spoke of aseptic loosening if the FDG uptake occurs in the bone-prosthesis interface with intensity less than or similar to the uptake of synovial structures/synovitis or soft tissues, and the diagnosis is infection if the uptake in the interface is much greater than in the synovial structures or soft tissues. Therefore, the difference between an aseptic and septic loosening is, for these authors, purely quantitative on a visual scale.

De Winter et al, 2001, have already explained how an increase in FDG uptake in the interface and the pseudocapsule around an implant with aseptic loosening is possible, due to its containing more activated macrophages and greater proliferation of fibroblast-like cells than the tissues around well attached prostheses. Of the 23 cases with painful prostheses evaluated by Manthey et al, with the first method, only 13 patients were operated on, and of these, a histological study was only obtained in 4 of them. The definitive diagnosis was verified in this study by “the surgical findings in the patients operated on and by follow-up to 2 years of patients who had not undergone surgery”. We consider that a good reference standard was not used for which we are certain that when synovitis is diagnosed, it is not a low profile infection, since patients with this diagnosis are not operated on and supposedly continue with the pain for which they sought medical advice (the authors do not say otherwise). Neither do we believe that it is easy to distinguish if this uptake in the interface or the periprosthetic (non-interface) uptake per se is infection or not, simply by assessment of the uptake by a visual scale; when we found high intensity uptake in the interface in our series, it was not always in septic mobilisations (fig. 3). In figure 4 we show an example of PET diagnostic failure with Manthey et al’s criteria in our series; the uptake pattern, according to Manthey et al, would correspond to synovitis and would concur in a FN, since this hip prosthesis was infected (positive biopsy and histopathology cultures).

In our study, furthermore, all the painful prostheses were considered as mobilised (macro or microscopically), and therefore we do not rely on that diagnosis of synovitis[40, 41] nor do we believe it, since it does not have a histopathologically confirmed basis.

We did not find a pattern characteristic of septic mobilisation as opposed to aseptic as proposed in the literature consulted[39, 40, 42, 43, 45, 50-53] in the form of high grade increased uptake in the bone-prosthesis interface (the biggest series recorded is that of Zhuang et al, 2001, with 36 mobilised TKPs and 38 mobilised THPs); moreover, neither the

number of areas nor the SUVmax contribute anything to this differential diagnosis. This last statement is supported by other studies on prostheses,[39, 43, 50, 54] and it had already been disclosed by Love et al (1994), who investigated pulmonary abnormalities,[55] and in studies on the detection of other types of infections. [48, 56, 57] That is, it would be false to think that the greater the number of uptake areas, the more possibility of infection. Neither would the premise that a higher SUVmax corresponds to infection be true. In fact, in our cases, the mean number of areas in THP is 3 for aseptic mobilisations and less, 2.7, for the septic mobilisations. The mean SUVmax was 3.9 (0-8.5) for the aseptic loosenings and 4.8 (2.6-13) for the septic, with the differences being not statistically significant and, moreover, not clinically valuable (mean difference of less than one unit for the SUVmax and the area).

We have not found a clear explanation for obtaining such low Se (4 FN) and Sp (5 FP) values with respect to the rest of the studies (table 5). Perhaps it is due to the learning curve and/or limited sample size, although it can be seen that the number of infections tested in all the series is around ten (maximum 21 combining hip and knees in Zhuang et al, 2001), so our series is along this line.

In our opinion, and reviewing the literature, it seems that ^{18}FDG-PET in the diagnosis of chronic musculoskeletal infections has greater diagnostic efficacy than the combination of bone scintigraphy + scintigraphy with labelled leukocytes,4 but in the case of prosthetic mobilisations, not only do we have to distinguish between whether there is infection or not, but since there is a third diagnostic category (1. infection; 2. no infection; 3. non-infected but mobilised prosthesis), it is not possible to establish a differential diagnosis with certainty; therefore we believe that there are other less costly tests with similar efficacy. This statement is supported by Love et al, 2001, who believe that although FDG imaging is exquisitely sensitive, it does not allow differential diagnosis in spite of the localisation. These results should not surprise us if we consider that FDG uptake is dependent on tissue metabolism. Inflammation and infection are both hypermetabolic states and, therefore, manifest as areas of increased activity. The combined image of a study with labelled leukocytes complemented by a bone marrow study (usually with ^{99m}Tc sulphur colloid) is superior to the FDG image, which in turn did not prove to be better than the combination of bone scintigraphy and Gallium citrate.[25, 26, 29, 32-34, 37, 39, 58-65]

CONCLUSIONS

The following conclusions emerged from our study:

1. ^{18}FDG-PET, in our series, did not prove to be an effective test in the presurgical diagnosis of prosthetic septic mobilisation.
2. We did not find a characteristic pattern of septic or aseptic prosthetic mobilisation in PET imaging.

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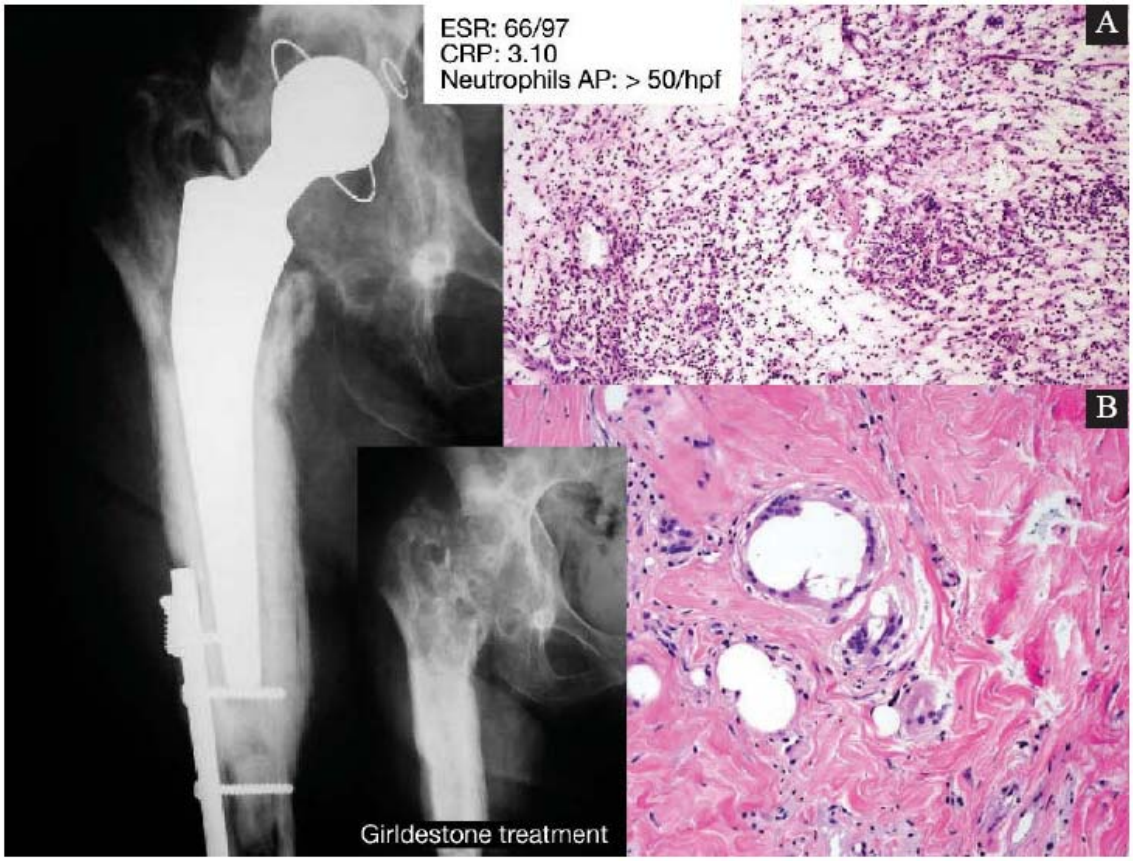

Figure 1. Images corresponding to the case of a prosthetic septic mobilisation after a first aseptic replacement. The clinical diagnosis, from radiographic and positron emission tomographic imaging and histopathology were clearly infection, although the cultures were negative. The biopsy shows abundant fibrin, granulation tissue with many neutrophils and detritus. Figure 1B shows giant cells with cement in their interior and macrophages.

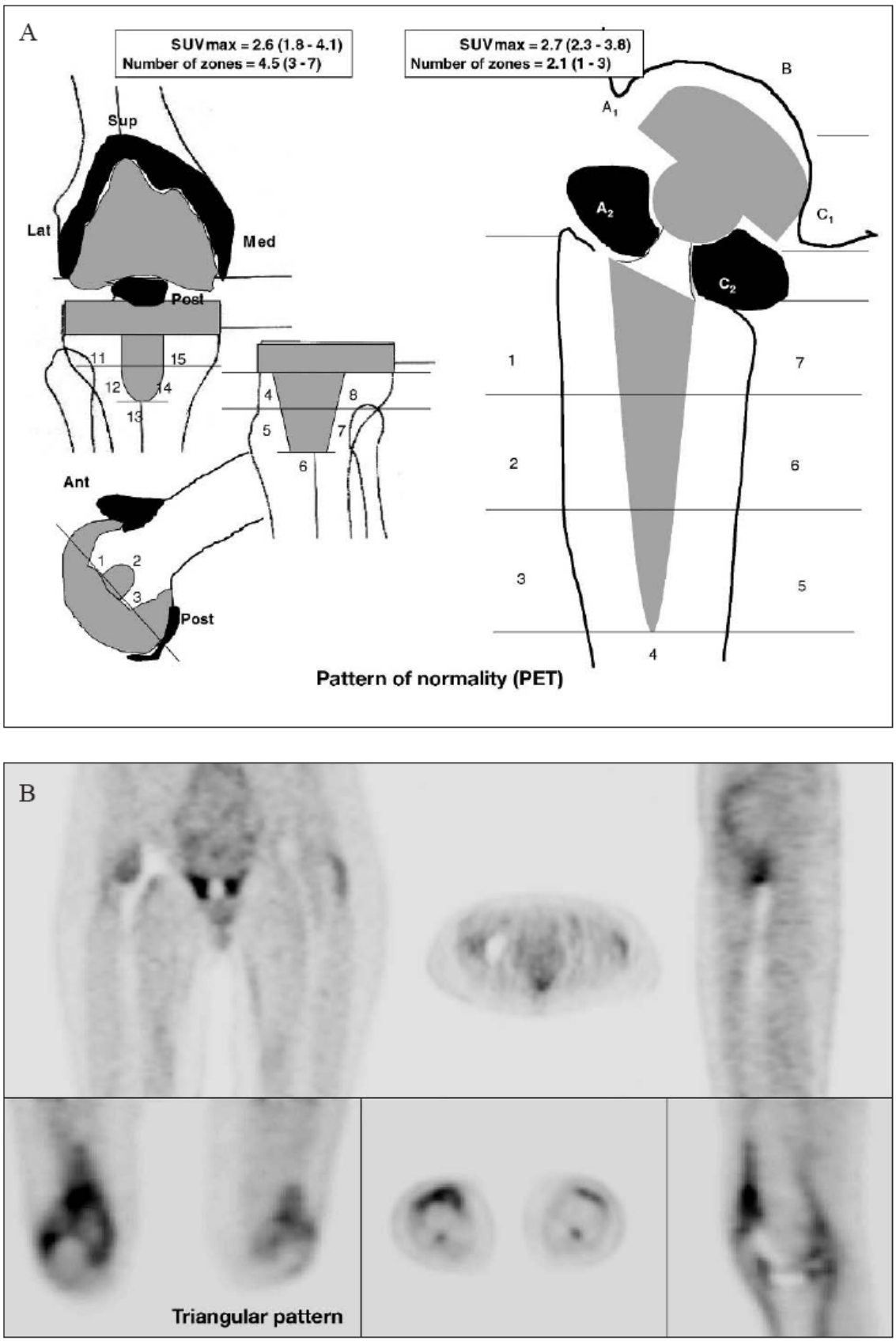

Figure 2. Pattern of normality of positron emission tomography (PET) in the hip (THP) and knee prosthesis (TKP) control group. 2A) Diagram taking the Gruen- DeLee areas for THP and Ewald areas for TKP as a base. 2B) Real test in the control group.

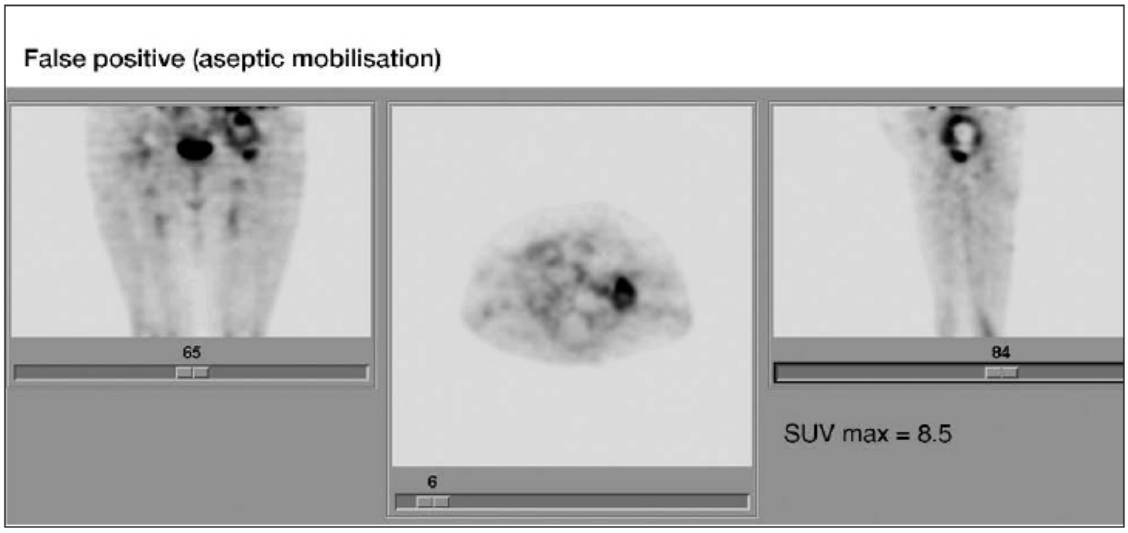

Figure 3. False positive on positron emission tomography (PET); case labelled as infected by PET imaging and which was not. SUVmax: maximum standardised uptake value.

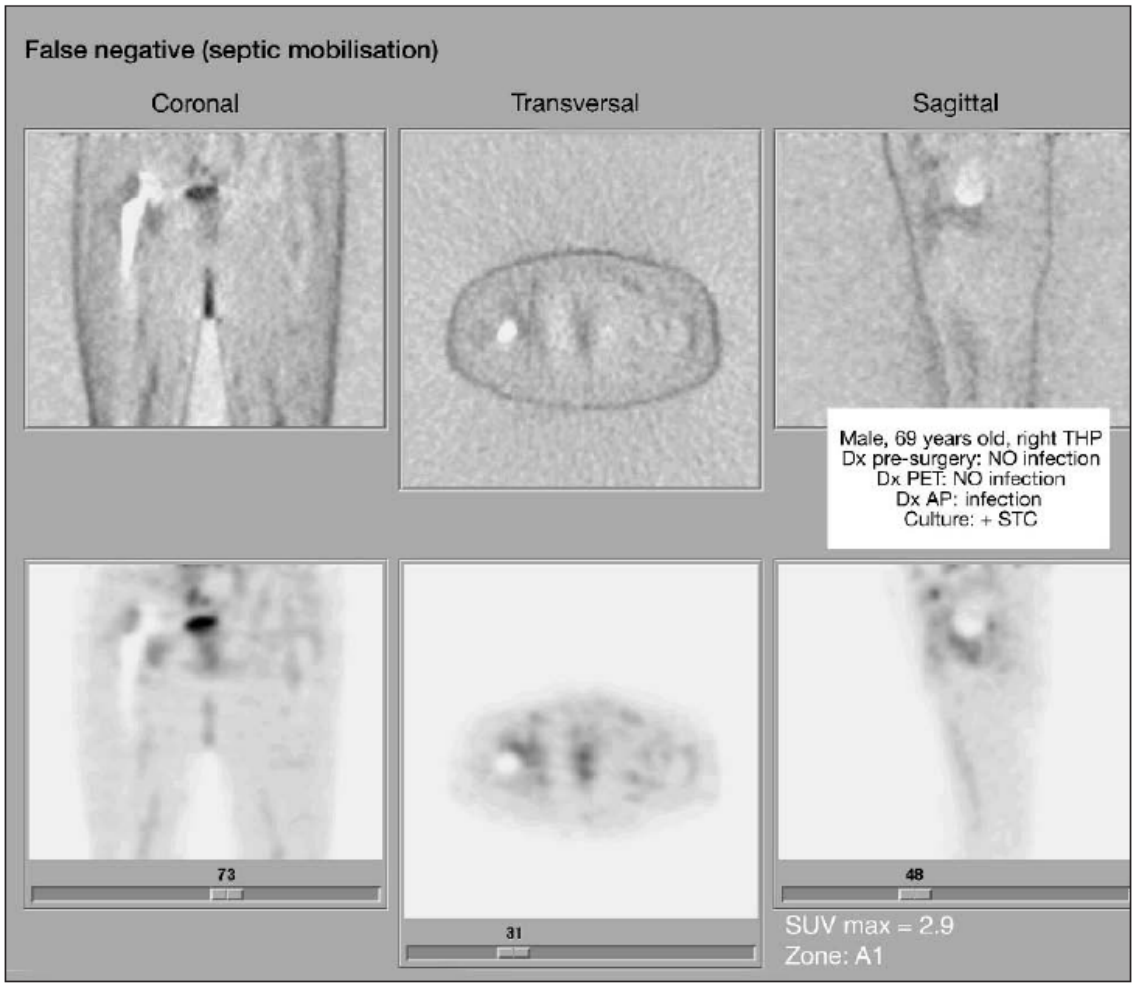

Figure 4. False negative on positron emission tomography (PET); case labelled as not infected by PET imaging and which was. THP: hip prosthesis; SUVmax: maximum standardised uptake value.

Table 1. Frequencies of uptake in cases of hip prosthesis on pet, distributed by areas (gray light: > 50%; gray dark: 25-50%)

Uptake zones/areas mobilisation	Aseptic mobilisation % (n = 13)	SUVmax % (n = 12[a])	Aseptic mobilisation % (n = 11)	SUVmax % (n = 11)	Control % (n = 11)
A1	46.2 (6/13)	16.7 (2/12)	18.2 (2/11)	9.1 (1/11)	0
B	30.8 (4/13)		9.1 (1/11)		0
C1	38.5 (5/13)	8.3 (1/12)	0		0
A2	84.6 (11/13)	16.7 (2/12)	100	27.3 (3/11)	100
C2	76.9 (10/13)	50 (6/12)	90.9 (10/11)	54.5 (6/11)	90.9 (10/11)
1	23.1 (3/13)		27.3 (3/11)		18.2 (2/11)
2	0		9.1 (1/11)	9.1 (1/11)	0
3	0		0		0
4	0		9.1 (1/11)		0
5	0		0		0
6	0		0		0
7	7.7 (1/13)		9.1 (1/11)		0
None	7.7 (1/13)	8.3 (1/12)	0		0

[a]In one of the aseptic mobilisations, only an emission study was carried out, so it was not possible to perform the quantification for the standardised uptake value. PET: positron emission tomography; SUVmax: maximum standardised uptake value.

Table 2. Frequencies of the number of pet uptake areas in the hip prosthesis case group, maximum standardised uptake value and statistical relationship between subgroups (septic/aseptic mobilisation)					
Type		**No. of areas THP**	**P**	**SUVmax THP**	**P**
Aseptic mobilisation	N	13		12	
	Mean	**3** (min 0, max 7)		**3.9** (min 0, max 8.5)	
	P_{25}	2		2.1	
	P_{50} **(median)**	**2**		**4.1**	
	P_{75}	4,50		5.20	
			0,955		0.740
Septic mobilisation	N	11		11	
	Mean	**2.7** (min 2, max 5)		4.8 (min 2.6, max 13)	
	P_{25}	2		2.9	
	P_{50} **(median)**	**3**		**4**	
	P_{75}	3		4.7	
PET: positron emission tomography SUVmax: maximum standardised uptake value THP: hip prosthesis					

Table 3. Definitive diagnosis versus PET[A] diagnosis					
		PET diagnosis by specialist			**Total definitive**
		No infection	**Possible infection**	**Certain infection**	
Definitive diagnosis	Aseptic mobilisation	8	1	4	13
	Septic mobilisation	4	2	5	11
Total specialist	12	3	9	24	
Sensitivity (Se) = 7/11 = 63.6 % (37.6 %; 85.6 %)					
Specificity (Sp) = 8/13 = 61.5 % (40.5 %; 84.3 %)					
Youden index = 0.25 (–0.05; 0.63)					
PET: positron emission tomography.					

Table 4. Statistical parameters of our study

	Sensitivity	Specificity	Youden index	PPV	NPV
Presurgical diagnosis[a]	78.6	100	0.79	100	97.45
Radiological periosteal detachment	64.3	76.5	0.41	25.05	94.69
^{18}FDG-PET	63.6	61.5	0.25	58.3	66.6
Neutrophil count (IBBF) > 5/hpf	78.57	100	0.79	100	97.45

[a]Clinical-radiological laboratory. IBBF: intra operative biopsy by freezing; NPV: negative predictive value; PPV: positive predictive value; ^{18}FDG-PET: positron emission tomography with fluorodeoxyglucose.

Table 5. Sensitivity and specificity of pet in the diagnosis of prosthetic infection[a]

Study	Cases	No.infections tested	Sensitivity	Specificity
Schnier et al,1998	34 (18 THP + 6 TKP)		100	95
Love et al, 2000	31 (PTC + PTR)	11	100	55
Zhuang et al, 2001	74 (total)	21	90,5	81,1
	38 (THP)	10	90 (9/10)	89.3 (25/28)
	36 (TKP)	11	91 (10/11)	72 (19/25)
Van Acker et al, 2001	21 (TKP)	6	100 (6/6)	73 (7/11)
Chako et al, 2002	41 (THP)	12	92 (11/12)	97 (28/29)
Cremerius et al, 2003	18 (THP)	7	86 (6/7)	91 (10/11)
Vanquickenborne et al, 2003	17 (THP)	8	87.5	77.8
García et al, 2004	31 (24 THP + 7 TKP)	14 (3 TKP + 11 THP)	**64.3 (9/14)**	**64.7 (11/17)**
	24 (THP)	11	**63.6 (7/11)**	**61.5 (8/13)**
	7 (TKP)	3	100 (3/3)	75 (3/4)

[a]Results obtained from the joint study of 24 THP and 7 TKP are included in these results. THP: hip prosthesis; TKP: knee prosthesis.